ISSN: 2519-7053 (Print)
ISSN: 2519-7878 (Online)

# NJHS

National Journal of Health Sciences

Vol. 10, No. 4,

2025

Quarterly

- *Breakthrough Pharmacotherapy Redefining Obesity Management*
- *E-Cigarette Use Linked to Significant Oral Health Complications*
- *Critical Gaps in VTE Prophylaxis for Pregnant Women*

NiBD Publications

www.njhsciences.com

NJHS
National Journal of Health Sciences

# Editorial Board


## Editorial Team

Patron-in-Chief
**Mr. Mohiuddin Chawla**

Editor-in-Chief
**Dr. Tabinda Ashfaq**
**MBBS, FCPS, FRCGP**
Outreach Clinical Lead, Department of Family Medicine, The Aga Khan University, Karachi, Pakistan.

Editor
**Dr. Tasneem Farzana**
**MBBS, MCPS, Dip Haem, FRCP (London)**
National Institute of Blood Disease & Bone Marrow Transplantation, Lahore Campus, Pakistan.

Managing Editor
**Muhammad Akif Ali Atif**

Founding Editor-In-Chief
**Dr. Tahir S. Shamsi (Late)**
**MBBS, MRCPath, FRCPath**
National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan.

## Advisory Board

**Dr. Fatima Riaz**
**MBBS, FCPS (Family Medicine), MRCGP (International) Family Medicine**
Department of Family & Community Medicine, College of Medicine, King Khalid University Abha, KSA

**Dr. S.H. Waqar**
**MBBS, FCPS, MCPS-HPE, FACS, CME**
PIMS and Federal Medical College, Islamabad, Pakistan.

**Dr. Tabinda Ashfaq**
**MBBS, FCPS, FRCGP**
Outreach Clinical Lead, Department of Family Medicine, The Aga Khan University, Karachi, Pakistan.

**Dr. Tasneem Farzana**
**MBBS, MCPS, Dip Haem, FRCP (London)**
National Institute of Blood Disease & Bone Marrow Transplantation, Lahore Campus, Pakistan.

## National

**Dr. Abdul Majeed Chaudhry**
**MBBS, FRCS, FCPS, MHPE, FCSSL, FASI**
Lahore Medical & Dental College, Lahore, Pakistan.

**Dr. Aizaz Mand Ahmad**
**MBBS, FCPS (Medicines), FCPS (Nephrology), FRCP (London)**
Evercare Hospital Lahore, Pakistan.

**Dr. Farid Ahmed**
**MBBS, FCPS, FRCS (UK)**
Alrazi Health care, Surgimed Hospital, Lahore, Pakistan.

**Dr. Nazish Saqlain**
**MBBS, FCPS (Haematology)**
Postgraduate Medical Institute/ Ameer-ud-din Medical College/ Lahore General Hospital, Lahore, Pakistan.

**Dr. Nazli Hossain**
**MBBS, FCPS (Obs & Gyne), MBE**
Dow University of Health Sciences, Karachi, Pakistan.

**Dr. Qamaruddin Baloch**
**MBBS, FCPS (Surgery)**
Al-Tibn Medical College & Hospital Isra University Karachi Campus, Pakistan.

**Dr. Rahat-Ul-Ain**
**MBBS, FCPS (Paeds), FCPS (Paeds/ Haem/Onco)**
The Children's Hospital and Institute of Child Health, Lahore, Pakistan.

**Dr. S.H. Waqar**
**MBBS, FCPS, MCPS-HPE, FACS, CME**
PIMS and Federal Medical College, Islamabad, Pakistan.

**Dr. Soufia Farrukh**
**F.C.P.S, F.R.C.S. (Glasgow)**
**Ophthalmology PGD & MSc (MED. EDU.)**
Quaid-e-Azam Medical College, Bahawalpur, Pakistan.

## International

**Dr. Gulali Aktas**
**MD, PhD (Internal Medicine)**
Department of Internal Medicine in Faculty of Medicine, Abant Izzet Baysal University, Golkoy, 14030, Bolu, Trkiye.

**Dr. Mohiuddin Ahmed Khan**
**MBBS, FCPS (Hematology, BCPS, FRCP)**
Department of Hematology, Dhaka Medical College Hospital, Dhaka, Bangladesh.

**Dr. Muhammad Akram**
**M.D., M.B.A., F.A.C.C., F.S.C.A.I.(Cardiology)**
Cardiac Center of Texas, USA.

**Dr Najam Us Saqib**
**M.B., B.S., DA (Eng.), FCARCS (Ire.)**
Doncaster & Bassetlaw NHS Foundation, Bassetlaw Hospital, United Kingdom.

**Dr. Suleman Atique**
**PhD (Biomed. Informatics)**
Department of Obstetrics and Gynecology, Oslo University Hospital (OUH), Rikshospitalet, Oslo, Norway.

## Editorial Secretariat

**Ms. Maria Baig**
Editorial Manager


Published under No. DC/EAST/HVC/Leg Br.24/2016 for NIBD Publications and printed at KAGZI Printers, Karachi, Pakistan.

Plot # 16, Maqbool Society, Block 7-8, Lal Muhammad Chaudhry Road, Karachi 75350, Pakistan.
(92 21) 34392398 & 34392399, www.njhsciences.com

**Note:** ORCID® is a registered trademark and the ORCID logo and iD icon are trademarks of ORCID, Inc.

NJHS
National Journal of Health Sciences

## About Us:

The National Journal of Health Sciences (NJHS) is the official publication of the National Institute of Blood Disease & Bone Marrow Transplantation (NIBD & BMT), Karachi, Pakistan. The journal serves as a dedicated platform for healthcare professionals, fostering the dissemination of substantial and credible contributions to the field of health sciences.

National Journal of Health Sciences publishes high-quality, peer-reviewed scholarly articles encompassing a wide range of research disciplines in both electronic and print formats. The journal offers an efficient and user-friendly submission system designed to facilitate a smooth and timely publication process. All submitted manuscripts undergo a rigorous double-blind peer review process, ensuring the highest standards of academic integrity and scientific excellence.

Each issue of National Journal of Health Sciences features clinically relevant and evidence-based research, readily accessible to the medical professionals, with the aim of advancing healthcare knowledge and fostering research development across the health sciences community.

## Vision Statement:

The National Journal of Health Sciences is committed to driving trans-formative progress in healthcare by fostering interdisciplinary collaboration, advancing equity in scientific dialogue, and promoting excellence in research dissemination.

We envision a future where high-quality, evidence-based knowledge serves as the foundation for measurable improvements in patient outcomes, healthcare systems, and population health worldwide.

## Mission Statement:

At National Journal of Health Sciences, our mission is to uphold the highest standards of ethical integrity and scholarly excellence in health sciences publishing. We provide an inclusive and dynamic platform for the dissemination of rigorously reviewed research, aligned with international best practices, including ICMJE, COPE, and EQUATOR guidelines.

Committed to fostering transparent scientific dialogue, we emphasize robust peer review, editorial integrity, and equitable access to knowledge. By championing innovation, diverse perspectives, and translational relevance, National Journal of Health Sciences empowers researchers and healthcare professionals to address critical health challenges and contribute to sustainable, evidence-based solutions that advance global healthcare.

## Disclaimer:

The content published in the National Journal of Health Sciences (NJHS), including but not limited to research articles, reviews, editorials, perspectives, letters to the editor, case reports, short communication reflects the views and opinions of the individual authors and does not necessarily represent the official position or endorsement of National Journal of Health Sciences, its Publisher, Editorial Board, Editors, or Editorial Staff. Authors are solely responsible for the accuracy, integrity, and originality of their submitted and published work, including all data, analyses, interpretations, and conclusions. This responsibility extends to ensuring compliance with ethical guidelines, research standards, and applicable laws, including those related to copyright, intellectual property, and data privacy.

### National Journal of Health Sciences, its Publisher, Editorial Board, Editors, and Editorial Staff disclaim any liability for:

**Errors or omissions:** We do not warrant the completeness or accuracy of the information published. **Consequences of use:** We shall not be held liable for any direct, indirect, incidental, consequential, or punitive damages arising from the use of or reliance on the content published in National Journal of Health Sciences. **Third-party content:** We are not responsible for the content of any external websites or resources linked to or referenced in the journal. **Ethical breaches:** Authors are responsible for ethical compliance, and National Journal of Health Sciences (NJHS) shall not be held liable for any ethical breaches committed by authors. **Legal liabilities:** We are not responsible for any legal issues that may arise from the publication of authors' content.

Authors warrant that their submissions are original, do not infringe upon the rights of others, and have not been previously published or are under consideration for publication elsewhere, except as disclosed in their submission. Authors agree to indemnify and hold harmless National Journal of Health Sciences, its Editorial Board, Editors, and Editorial Staff from any claims, liabilities, or expenses arising from their published work.

By submitting a manuscript to National Journal of Health Sciences, authors acknowledge that they have read, understood, and agreed to this disclaimer and its terms. This disclaimer is subject to change without notice.

NJHS
National Journal of Health Sciences

# Table of Content
Volume 10, Issue 4, 2025

## Editorial

**220 Transforming Obesity Care: Medications at the Forefront**

*Tabinda Ashfaq*

## Research Articles

**222 Association of E-Cigarette Use and Oral Health Complications: A Cross Sectional Study in Punjab, Pakistan**

*Muhammad Taaha, Naila Umer, Hafiz Danish Altaf, Rabia Anjum, Hammad Hassan, Safi Ullah Khan*

**230 Is Obesity Associated with a Higher Risk of Differentiated Thyroid Cancer in a Cytologically Proven Series of Thyroid Nodules?**

*Irfan Ahmed Shaikh, Danish Ur Rehman, Sidra Bano, Rajesh Kumar, Ramsha Khalid, Raheem Bakhsh*

**238 Diagnostic Accuracy of Ultrasound in Detecting Axillary Lymph Nodes in Patients with Early Breast Cancer Taking Histopathology as a Gold Standard**

*Ambreen Shaikh, Saleha Anwar, Hasnain Ali, Raisa Altaf Malik, Humaira Erum, Bisma Rizwan*

**244 Role of Heparin to Prevent Hypertrophic Scarring in Donor Area of Split Thickness Skin Graft**

*Asma Ishtiaq, Faisal Akhlaq Ali Khan, Farhan Zahid, Iqra Muhammad Tasleem, Asra Zahid, Nasreen Bano Khatri*

**251 Outcomes of Intestinal Anastomosis with or without Platelet Rich Plasma Application**

*Syeda Wajiha Mustafa, Malik Asad Munir, Atika Tahir, Batool Fatima, Muhammad Azam Mirza, Muhammad Kashif Bashir*

**258 Risk Assessment of Venous Thromboembolism in Pregnancy and Adequate Prophylaxis: An Observational Study**

*Aliya Nasim, Sagheera Anjum Manaver, Naima Shah, Humaira Tahir, Mehvish Kanval*

**264 Experience in Pediatric Bleeding Disorders in Tertiary Care Health Services from Southern Region of Saudi Arabia: Single Center Retrospective Study**

*Badriah Gharamah Al Asmari, Ali Mujtaba Tahir, Mohammed Alpakra, Mohaned Mustafa Ahmed Mohammad, Sara Saeed Mahamoud Hassanien, Mahnoor Saeed, Manea Abdullah Alqarni, Sami Saleh Alamri*

**271 Prevalence of Depression and Anxiety in Patients with Obstructive Lung Disease and Correlation with Spirometry**

*Ehab Nabeel, Sohail Akhtar, Ahmed Ali, Syed Wajahat Hussain, Mujahid Hussain*

**279 In-Hospital Outcomes of Early Extubation in Post CABG Patients: A Retrospective Study from a Tertiary Care Hospital in Karachi, Pakistan**

*Qaiser Aziz Khan, Latifa Haidari, Imran Khan Sandeelo, Marium Nastaeen Sarhandi, Sarib Bin Yasir, Mariam Amir*

**287 Knowledge, Attitudes & Perceptions towards Premenstrual Syndrome among Low Socioeconomic School-Going Adolescent Girls in Karachi, Pakistan**

*Shaikh Ali Masood, Shabbir Ahmed Mallick, Hamna Jamal, Maria Murtaza, Manahil Nadeem, Ameera Shabbir*

**292 Timing of Surgical Intervention and its Impact on Short-term Outcomes in Pediatric Hydrocephalus**

*Shakeel Ahmed, Shoaib Saleem Khan, Syed Zahid Hussain Shah, Muhammad Ali Waqas, Ubaid Ullah, Zeeshan Karim*

## Case Report

**299 Spontaneous Resorption of Mandible in a Middle Aged Female**

*Hafiz Muhammad Bilal Siddiqui, Hafiz Murtaza Hussain, Talha Ahmed Qureshi, Mariam Mubashir*

Research Article

# Role of Heparin to Prevent Hypertrophic Scarring in Donor Area of Split Thickness Skin Graft

Asma Ishtiaq*, Faisal Akhlaq Ali Khan, Farhan Zahid, Iqra Muhammad Tasleem, Asra Zahid, Nasreen Bano Khatri

*Department of Plastic & Reconstructive Surgery, Dr. Ruth K.M. Pfau Civil Hospital, Karachi, Pakistan.*

**Abstract: Background:** It is normal to experience hypertrophic scarring after skin harvesting at donor site. Topical heparin treatment has been suggested to have particular significance in the treatment of hypertrophic scars.

**Objective:** to determine the effect of topical heparin for prevention of hypertrophic scars and pain status following split thickness skin graft donor site.

**Materials and Methods:** This open label randomized control trial (NCT07196358) was performed at Plastic & Reconstructive Surgery Department, Ruth K.M. Pfau Civil Hospital, Dow University of Health Sciences during 1st August, 2024 to 31st July, 2025. Group H was assigned to heparin group whereas Group C was assigned to control group. Study outcomes included pain status, additional postoperative analgesic requirement and hypertrophic scarring. Patients were assessed at 14 days, 4 weeks, 6 weeks, 2 months and 3 months following the procedure.

**Result:** A total 50 patients were studied in each group. Post-operative analgesic consumption was significantly lower in patients managed with heparin than control group ($p<0.001$). Throughout the study period pain was significantly lower in heparin group than control group. At second month and third month, occurrence of hypertrophic scarring frequency was significantly higher in control group than heparin group. The mean VSS score was significantly lower in heparin group than control group.

**Conclusion:** The findings suggests that heparin was found to be superior in comparison to the conventional approach of sterile paraffin dressing soaked with normal saline in terms of pain control and prevention of hypertrophic scarring.

**Keywords:** Donor site, Hypertrophic scarring, Heparin, Numeric rating scale, Vancouver scar scale, Split thickness skin graft.

## INTRODUCTION

Split thickness skin graft (STSG) are categorized as thin, intermediate and thick for thickness of 0.15 to 0.3mm, 0.3 to 0.45mm, and 0.45 to 0.6m respectively. Due to preservation of dermis and dermal appendages, STSG donor sites usually regenerate new skin within two to three weeks. Because donor sites can be reused if suitable healing has occurred, STSGs are advantageous in burn surgery and big wounds with a scarcity of donor sites [1-3].

It is normal to experience wound contracture and aesthetic problems, such as variations in pigmentation and texture between the skin-graft and donor site. The donor site of a split-thickness skin graft is often scarred or discolored, even though it can heal on its own [4].

The scars are caused by deviations from the typical processes of cutaneous wound healing [5]. Excessive scarring can considerably diminish quality of life of affected individuals as it leads to itching, discomfort and limited mobility [6]. After a traumatic skin injury, wound infection, or wound closure involving excessive tension, hypertrophic scarring typically develops 4 to 8 weeks later [7]. Multiple clinical studies reported 40-94% incidence of hypertrophic scarring following surgery whereas it varies from 30-91% in burn injuries [8].

Many invasive and non-invasive therapeutic methods are available to improve the appearance of scars. These alternatives include topical silicone gel, intralesional corticosteroids (triamcinolone), compression or pressure therapy, radiation, and cryotherapy [9, 10]. The side effects of these treatments vary (for example, radiation therapy can cause basal cell carcinoma, while corticosteroid therapy might cause hyperpigmentation) [11] and in a resource poor country most of these modalities are expensive. Lately, topical treatments have come to be seen as the primary means of managing and preventing hypertrophic scars [12].

Due to its anti-inflammatory properties, fibroblast anti-proliferative activity, suppression of proteoglycan and collagen synthesis, loosening of collagen structure, and enhancement of scar

* Address correspondence to this author at the Department of Plastic & Reconstructive Surgery, Dr. Ruth K.M. Pfau Civil Hospital, Karachi, Pakistan. Email: asma.kk76@gmail.com

 © 2025 NIBD Publications 

elasticity, topical heparin treatment has been suggested to have particular significance in the treatment of hypertrophic scars [13]. Additionally, heparin has a potent anticoagulant effect that can enhance local blood circulation and avoid microcirculation thrombosis [14]. Studies support the topical application of heparin to promote wound healing and has been investigated in the past and has yielded significant results [15-17].

Researches have been conducted on burn victims, supporting the topical application of heparin for wound healing [15-17]. There is, however, limited work done on prevention of hypertrophy at the donor location after STSG. This study aims to determine the effect of topical heparin for prevention of hypertrophic scars and pain status following split thickness skin graft donor sites. In a resource poor country an inexpensive modality for management of hypertrophic scars would be a crucial breakthrough and reinforce a change in practice.

## MATERIALS AND METHODS

This open label randomized control trial was performed at Plastic & Reconstructive Surgery Department, Ruth K.M. Pfau Civil Hospital, Dow University of Health Sciences. The study was performed during 1st August, 2024 to 31st July, 2025 with the approval of Institutional Review Board (IRB-3459/DUHS/Approval/2024/185). The trial was registered with the number NCT07196358. Patients of age 18 years and above of either gender, requiring STSG with albumin of >3 and providing their consent to participate were included. Patients allergic to heparin, having with diabetes, any hematological disorders, kidney and liver diseases and with malignancies, taking medications impacting healing time and having hypertrophic scaring prior to the study were excluded.

Sample size was estimated with an approach of two proportion sample size calculation. From existing literature, reported frequency of hypertrophic scarring in heparin treated group was 10% and 64% in control group. At power of 80% and 95% confidence interval, the yielded sample size was lower than 30. Thus for better study results, we enrolled 50 patients per group. Patients were enlisted consecutively followed by random group allocation using sequentially numbered opaque sealed envelope [18-21].

Patients requiring split thickness skin graft were admitted a day before and their medical fitness assessed as per hospital protocol. Marking at donor site was done before moving patients to operation theatre (OT). After patients shifting the patients to holding area, they were allocated to the study groups using sequentially numbered opaque sealed envelope protocol. Group H was assigned to heparin group whereas Group C was assigned to control group. Patients were shifted to OT where skin was harvested for STSG using Humby's knife. After harvesting graph at donor site, a heparin dressing was immediately applied. 5 ml of 5000 IU/ml heparin solution was mixed with 50 ml normal saline solution for preparing 55 ml of 500 IU/ml concentration heparin sodium solution (heparin). This diluted heparin solution was then evenly dropped on the gauze piece intended to be placed at donor site. A standard dressing of sterile paraffin gauze humidified with 0.9% normal saline was applied in control group. After operation patients were kept in holding area for two hours and then shifted to ward. Paracetamol 15mg/Kg every 8 hourly (maximum 1gm per dose) was administered as per protocol for pain management. Additional analgesia ketorolac 30 mg IV was administered on demand. Patients were discharged next of the procedure as per hospital protocol.

Patients underwent follow-up appointments in the outpatient clinic at specific time points of 14 days, 4 weeks, 6 weeks, 2 months and 3 months following the procedure. They were instructed to come in earlier than an actual follow-up visit for any wound concerns such as excessive pain, discharge, redness, saturation of the dressing and other symptoms of concern.

Study outcomes included pain status, additional postoperative analgesic requirement and hypertrophic scarring. Study outcomes included pain status, additional analgesic requirement postoperatively, hypertrophic scarring. Pain was assessed using Numeric Rating Scale (NRS) which a ten-point is ranging from 0-10, with 0 being no pain at all and 10 indicating worst pain [22]. Additional analgesia was administered on patient demand or if pain score was higher than 5 or above. Hypertrophic scarring was assessed using Vancover Scar Scale (VSS). VSS evaluates four parameters including vascularity, height, pliability, and pigmentation. The score ranges from 0-13 [23]. An increase of 25% in total i.e. >3 or a height score of ≥1 was used as a criteria for hypertrophic scarring assessment [24].

## STATISTICAL ANALYSIS

Data was analyzed using SPSS version 27. Frequencies and percentages were computed for categorical variables. Numerical variables were summarized as mean ± standard deviation after assessing normality with Shapiro-Wilk test. Chi-square test was applied to compare categorical variables. Two-way repeated measure ANOVA was applied to compare changes in pain and VSS score over the between the two groups. Main effects of group and time were evaluated as well interaction of these two. Sphericity assumption was checked using Mauchly's was tested prior to running test. Statistical significance was defined based on two tailed p-value at ≤0.05.

## RESULT

A total of 50 patients were studied in each group. Patients did not differ on the basis of confounding variables such as age (p=0.517), gender (p=1.000), indication of STSG (p=0.472) and graft size (p=0.877) (Table **1**).

**Table 1.** Summary of Demographic and Clinical Features among Two Groups.

| Variables | Group H n(%) | Group C n(%) | p-value |
|---|---|---|---|
| Age (in years)# | 32 ± 10.4 | 30.6 ± 9.6 | 0.517 |
| Graft size (in cm) | 10.5 ± 1.8 | 10.6 ± 2.1 | 0.877 |
| **Gender** | | | |
| Male | 35(70) | 34(68) | 1.000 |
| Female | 15(30) | 16(32) | |
| **Clinical Indication** | | | |
| Thermal burn | 10(20) | 11(22) | 0.472 |
| Traumatic skin loss secondary to RTA | 10(20) | 13(26) | |
| Donor site of flaps | 11(22) | 7(14) | |
| Scalp deglove wounds | 3(6) | 8(16) | |
| Post debridement necrotizing soft tissue infection | 6(12) | 5(10) | |
| Excision of tumors on chest and abdominal walls | 6(12) | 5(10) | |
| Post burn contractures | 4(8) | 1(2) | |

#: Numerical variables are presented as mean ± SD.

Table **2** shows comparison of postoperative stay and analgesic consumption among the study groups. Patients treated with heparin and conventional had not significant different in terms of postoperative stay (p=0.607). Analgesic consumption was significantly lower in patients managed with heparin than control group (p<0.001).

**Table 2.** Comparison of Postoperative Stay and Analgesic Consumption among the Study Groups.

| Variables | Group H mean ± SD | Group C mean ± SD | p-value |
|---|---|---|---|
| Post-operative stay | 1.2 ± 0.4 | 1.4 ± 0.5 | 0.607 |
| Analgesic consumption | 13.7 ± 4.2 | 28.3 ± 5.9 | *<0.001 |

*Significant at p<0.05.

Table **3** displays pain status among the two study groups throughout the study. Two way RM ANOVA showed that there was significant main effect of time with decrease in pain over the time (F=313.6, p<0.001, $\eta^2$=0.862). A significant effect of groups showed that pain was significantly lower in Group H than Group C time (F=188.5, p<0.001, $\eta^2$=0.741. Group and time interaction was significant time (F=27.3, p<0.001, $\eta^2$=0.428) showing pain quickly dropped in Group H.

**Table 3.** Two Way Repeated Measure ANOVA Analysis for Pain Scores Over the Time between the Study Groups.

| Variables | Group H | Group C | Time | | Group | | Interaction | |
|---|---|---|---|---|---|---|---|---|
| | mean ± SD | mean ± SD | Partial $\eta^2$ | p-value | Partial $\eta^2$ | p-value | Partial $\eta^2$ | p-value |
| At 24 hours | 4.8 ± 1.7 | 8.3 ± 2.4 | 0.862 | <0.001 | 0.741 | <0.001 | 0.428 | <0.001 |
| At 14 days | 3.4 ± 0.8 | 4.1 ± 1.4 | | | | | | |
| 4 weeks | 1.8 ± 0.9 | 3.2 ± 1.2 | | | | | | |
| 6 weeks | 1.2 ± 0.6 | 2.4 ± 0.7 | | | | | | |
| 2 months | 0.7 ± 0.1 | 1.6 ± 0.5 | | | | | | |
| 3 months | 0.5 ± 0.1 | 1.1 ± 0.4 | | | | | | |

Table **4** outlines comparison of hypertrophic scarring among the study groups. Frequency of hypertrophic scarring was not significantly different among Group H and Group C at 4 weeks (p=0.617) and 6 weeks (p=0.160). At second month and third month, occurrence of hypertrophic scarring frequency was significantly higher in control group than heparin group.

**Table 4.** Comparison of Hypertrophic Scarring among the Study Groups.

| Variables | Group H n(%) | Group C n(%) | p-value |
|---|---|---|---|
| At 24 hours | - | - | - |
| At 14 days | - | - | - |
| 4 weeks | 1(2) | 3(6) | 0.617 |
| 6 weeks | 2(4) | 7(14) | 0.160 |
| 2 months | 2(4) | 10(20) | *0.014 |
| 3 months | 4(8) | 15(30) | *0.005 |

*Significant at p<0.05.

Table **5** shows comparison of Vancouver scar scale among the study groups. Two way RM ANOVA showed that there was significant main effect of time with reduction in VSS over the time ($F=156.8$, $p<0.001$, $\eta^2=0.725$). A significant effect of groups showed that VSS was significantly lower in Group H than Group C time ($F=223.4$, $p<0.001$, $\eta^2=0.634$. Group and time interaction was also significant time ($F=36.2$, $p<0.001$, $\eta^2=0.518$).

**Table 5.** Two Way Repeated Measure ANOVA Analysis for Vancouver Scar Scale Scores over the time between the Study Groups.

| Variables | Group H | Group C | Time | | Group | | Interaction | |
|---|---|---|---|---|---|---|---|---|
| | | | Partial $\eta^2$ | p-value | Partial $\eta^2$ | p-value | Partial $\eta^2$ | p-value |
| At 24 hours | - | - | - | - | - | - | - | - |
| At 14 days | - | - | - | - | - | - | - | - |
| 4 weeks | 1.4 ± 0.7 | 2.6 ± 1.3 | 0.725 | <0.001 | 0.634 | <0.001 | 0.518 | <0.001 |
| 6 weeks | 2.1 ± 1.1 | 4.1 ± 1.2 | | | | | | |
| 2 months | 3.2 ± 1.4 | 5.3 ± 1.7 | | | | | | |
| 3 months | 3.5 ± 1.6 | 6.4 ± 1.7 | | | | | | |

## DISCUSSION

We examined the impact of topical heparin on both pain and the development of hypertrophic scarring after harvesting skin from the donor site of a split-thickness skin graft (STSG). Our data show that patients receiving topical heparin experienced overall lower pain scores and even lower rates of hypertrophic scarring than patients who received standard care. Hypertrophic scarring was observed in 30% of control patients compared with 10% of heparin-treated patients at 3 months; moreover, pain scores in heparin treated patients were lower at every follow-up time point (14 days, 4 weeks, 6 weeks, 2 months, and 3 months) than control patients.

Post-surgical pain in the donor site is a noted source of patient discomfort and adds to the requirement of analgesia [25]. In our whole group, mean NRS pain scores were lower for both time points in the heparin group compared to the no-heparin group, especially in the first month. These findings relate to earlier studies that observed analgesia or relief of discomfort for topical heparin in superficial burns or donor sites. For example, Masoud M. and coworkers indicated that topical heparin relieved pain and reduced the need for analgesics in patients with acute burn injury [19]. Similarly, Mohamed *et al.* found topical heparin was associated with reduced pain in facial burn wounds [26]. Moreover, Adil *et al.* showed that topical heparin spray improved donor comfort [27]. These findings support the hypothesis that heparin's anti-inflammatory effects through the modulation of microcirculation reduction in local edema may lead to pain relief early and later in the postoperative period at donor sites.

Hypertrophic scarring at STSG donor sites is a well-known late complication, associated with excessive fibroblast proliferation and collagen deposition [28]. We observed hypertrophic scarring at a minimum of 4 weeks, with increasing incidence from 6-8 weeks and peak incidence at 3 months. After 3 months, hypertrophic scarring was apparent in 30% of the control group, and only 10% of the heparin group. Given insufficient studies, comparisons to previous literature are limited, as few clinical studies have examined topical heparin specifically for prevention of hypertrophic scarring at STSG donor sites. Adil *et al.* [27] reported improved healing of the donor site with topical heparin spray, as well as decreased scar severity, however, they did not provide a comparative hypertrophic scar rate that would be appropriate for comparison to the heparin group [1]. Masoud *et al.* [19] and Mohammed *et al.* [26] discussed improved wound healing, since the investigated heparin-containing treatments, but did not focus on hypertrophic scarring at the STSG donor site [19, 26].

Since limited literature was existing on the topic of interest and few studies were available for direct comparison. As a result, we

supported our discussion by reviewing animal studies as well as studies with heparin containing forms of other wound types. For example, in a full-thickness burn rat model, Yergoz *et al.*, showed that heparin-mimetic peptide nanofiber gels enhanced regeneration while minimizing fibrosis [29]. Mohammadi Sardo *et al.* hypothesized that heparinized suture threads may help diminish scar formation through the modulation of fibroblast activity [30]. Furthermore, studies using heparin-containing topical products, such as Contractubex® in rabbits, have demonstrated significant reductions in hypertrophic scar formation following primary closure of a wound [31]. Taken together, these studies corroborated our findings, and provide a mechanistic rationale for the reduction in scarring that we observed in the heparin group, notwithstanding the lack of direct comparative studies of SCSG donor sites in humans.

In our study, the Vancouver Scar Scale (VSS) scores reflected the same trends for rates of hypertrophic scars. At the 3-month time period, the mean VSS was 6.0 ± 1.8 in the control group and 3.5 ± 1.4 in the heparin group. The heparin group exhibited lower VSS scores as early as 4 weeks after application, which suggests the heparin group had reduced thickness, vascularity, and improved pliability. These results support previous work demonstrating that heparin has anti-fibrotic effects [19, 26, 27] and further supports early application of heparin during the remodeling phase to help improve the quality of the scar. Additionally, patients in the heparin group reported lower itch and tightness scores, which indicate an improvement that could be of clinical significance and improve patient comfort.

From a clinical standpoint, topical heparin offers the benefits of easy application, low cost, and excellent safety. The results support the idea that heparin could be integrated into the routine care of the donor site to improve patient comfort, reduce the need for systemic analgesics, and decrease the likelihood of developing hypertrophic scarring. This appears particularly relevant in sites where donor site morbidity is high or follow-up compliance is low.

## LIMITATIONS

Some limitations must be considered. First, the sample size was relatively small (50 patients in each group) and may also limit statistical power and generalizability. Second, the follow-up period was limited to 3 months, as hypertrophic scars can continue to mature after this period and longer follow-up would provide a complete profile of the scar evolution. Third, pain and scar assessments were made using validated scales (NRS and VSS), but those remain partially subjective and subject to patient perception or assessor variability. Fourth, direct human studies never compared hypertrophic scarring at STSG donor sites with topical heparin. Comparisons were made from animal studies, and/or animal studies on heparin. Fifth, blinding was not possible in this study. These studies provided indirect comparisons, as they are not done in the same setting or microenvironment as human donor sites. Finally, we did not stratify by skin type, comorbidities, or anatomical site or other factors that might influence healing and scar formation. Additionally, this study was conducted at a single center, which may limit external validity.

## CONCLUSION

The findings suggests that heparin was found to be superior in comparison to the conventional approach of sterile paraffin dressing soaked with normal saline in terms of pain control and prevention of hypertrophic scarring.

## ABBREVIATIONS

**NRS**: Numeric Rating Scale.

**OT**: Operation Theatre.

**STSG**: Split Thickness Skin Graft.

**VSS**: Vancouver Scar Scale.

## AUTHORS' CONTRIBUTION

**Asma Ishtiaq**: Conceptualization, Study Design, Writing Draft, Final approval, final proof to be published.

**Faisal Akhlaq Ali Khan** and **Farhan Zahid**: Study Design, Critical review and revision the manuscript.

**Iqra Muhammad Tasleem** and **Asra Zahid**: Writing Draft.

**Nasreen Bano Khatri**: Methodology, Data analysis and interpretation.

## ACKNOWLEDGEMENTS

Declared none.

## ETHICAL DECLARATIONS

### Data Availability Statement

All of the collected data is presented in the manuscript.

### Ethical Approval

The study was executed after formal approval from Institutional Review Board of Dow University of Health Sciences (IRB-3459/DUHS/Approval/2024/185).

### Clinical Trail Registry

This study was registered with ClinicalTrials.gov under identifier NCT07196358 (https://clinicaltrials.gov/study/NCT07196358).

### Consent to Participate

A written informed consent was sought from all patients prior to their participation.

### Consent for Publication

All authors provide consent for publication of this work.

### Conflict of Interest

Declared none.

### Competing Interest / Funding

None.

### Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

## REFERENCES

[1] Braza ME, Fahrenkopf MP. Split-Thickness Skin Grafts. Treasure Island (FL): StatPearls Publishing 2024; Available from: https://www.ncbi.nlm.nih.gov/books/NBK551561/. [Updated 2023 Jul 25].

[2] Kern JN, Weidemann F, O'Loughlin PF, Krettek C, Gaulke R. Mid- to long-term outcomes after split-thickness skin graft vs. skin extension by multiple incisions. In Vivo 2019; 33(2): 453-64.

[3] Ayaz M, Najafi A, Karami MY. Thin split thickness skin grafting on human a cellular dermal matrix scaffold for the treatment of deep burn wounds. Int J Organ Transplant Med 2021; 12(1): 44-51.

[4] Jang YC. Split-thickness skin grafting. In: The Art of Skin Graft: Advanced Graft Technique. Singapore: Springer Nature Singapore 2024; pp. 1-50.

[5] Ogawa R. Update on hypertrophic scar management in burn patients. Clin Plast Surg 2024; 51(3): 349-54.

[6] Har-Shai Y, Har-Shai L. Minimally invasive technologies for the treatment of hypertrophic scars and keloids: Intralesional cryosurgery. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, Eds. Textbook on Scar Management: State of the Art Management and Emerging Technologies. Cham (CH): Springer 2020; pp. 235-41.

[7] Anderson JB, Foglio A, Harrant AB, Huang CA, Hultman CS, Mathes DW, *et al.* Scoping review of therapeutic strategies for keloids and hypertrophic scars. Plast Reconstr Surg Glob Open 2021; 9(3): e3469. DOI: 10.1097/GOX.0000000000003469.

[8] Shirakami E, Yamakawa S, Hayashida K. Strategies to prevent hypertrophic scar formation: A review of therapeutic interventions based on molecular evidence. Burns Trauma 2020; 8: tkz003. DOI: 10.1093/burnst/tkz003.

[9] Jackson K, Lee A, Ahmad N, Nguyen HP. Analysis of therapeutic interventions for hypertrophic and keloid scarring: A systematic review. J Drugs Dermatol 2025; 24(8): 770-6. DOI: 10.36849/JDD.8895.

[10] Salem SAM, Abdel Hameed SM, Mostafa AE. Intense pulsed light versus cryotherapy in the treatment of hypertrophic scars: A clinical and histopathological study. J Cosmet Dermatol 2021; 20(9) :2775-84. DOI: 10.1111/jocd.13971.

[11] Meaume S, Le Pillouer-Prost A, Richert B, Roseeuw D, Vadoud J. Management of scars: Updated practical guidelines and use of silicones. Eur J Dermatol 2014; 24(4): 435-43. DOI: 10.1684/ejd.2014.2356.

[12] Hassanpour SE, Farnoush N, Karami MY, Makarem A. The effect of silicone gel versus contractubex gel on the upper-extremity postsurgical scars: A randomized, double-blinded, controlled trial. Med J Islam Repub Iran 2020; 34: 146.

[13] Murakami T, Shigeki S. Pharmacotherapy for keloids and hypertrophic scars. Int J Mol Sci 2024; 25(9): 4674. DOI: 10.3390/ijms25094674.

[14] Bissacco D, Pisani C, Avallone G, D'Alessio I. Topical heparin and heparinoid-containing products as treatments for venous disorders: compounds, effects, clinical implications, and recommendations. J Clin Med 2025; 14(6): 1859. DOI: 10.3390/jcm14061859.

[15] Vijayakumar C, Prabhu R, Senthil Velan M, Muthu Krishnan V, Kalaiarasi R, Swetha T. Role of heparin irrigation in the management of superficial burns with special reference to pain relief and wound healing: A pilot study. Cureus 2018; 10(8): e3157.

[16] Olczyk P, Mencner Ł, Komosinska-Vassev K. Diverse roles of heparan sulfate and heparin in wound repair. BioMed Res Int 2015; 2015: 549417.

[17] Peng J, Zhao H, Tu C, Xu Z, Ye L, Zhao L, *et al.* In situ hydrogel dressing loaded with heparin and basic fibroblast growth factor for accelerating wound healing in rat. Mater Sci Eng C Mater Biol Appl 2020; 116: 111169.

[18] Das S, Mitra K, Mandal M. Sample size calculation: Basic principles. Indian J Anaesth 2016; 60(9): 652-6. DOI: 10.4103/0019-5049.190621.

[19] Masoud M, Wani AH, Darzi MA. Topical heparin versus conventional treatment in acute burns: A comparative study. Indian J Burns 2014; 22(1): 43-50.

[20] Rotatori RM, Starr B, Peake M, Fowler L, James L, Nelson J, *et al.* Prevalence and risk factors for hypertrophic scarring of split thickness autograft donor sites in a pediatric burn population. Burns 2019; 45(5): 1066-74. DOI: 10.1016/j.burns.2019.02.003.

[21] DOIg GS, Simpson F. Randomization and allocation concealment: A practical guide for researchers. J Crit Care 2005; 20(2): 187-91; discussion 191-3. DOI: 10.1016/j.jcrc.2005.04.005.

[22] Childs JD, Piva SR, Fritz JM. Responsiveness of the numeric pain rating scale in patients with low back pain. Spine 2005; 30: 1331-4.

[23] Baryza MJ, Baryza GA. The vancouver scar scale: An administration tool and its interrater reliability. J Burn Care Rehabil 1995; 16(5): 535-8.

[24] Thompson CM, Sood RF, Honari S, Carrougher GJ, Gibran NS. What score on the vancouver scar scale constitutes a hypertrophic scar? Results from a survey of North American burn-care providers. Burns 2015; 41(7): 1442-8. DOI: 10.1016/j.burns.2015.04.018.

[25] Sinha S, Schreiner AJ, Biernaskie J, Nickerson D, Gabriel VA. Treating pain on skin graft donor sites: Review and clinical recommendations. J Trauma Acute Care Surg 2017; 83(5): 954-64. DOI: 10.1097/TA.0000000000001615.

[26] Mohamed NG, Abolnaga AM, Moghazy AM, Gomaa AA. Comparison between topical beta-sitosterol and topical hirudin in management of facial burns. Egypt J Plast Reconstr Surg 2024; 48(1): 7-15.

[27] Adil F, Memon MA, Khan FAA, Awan A, Siddiqui SU, Piprani FZ, *et al.* Efficacy of topical heparin spray on donor site wound healing after split thickness skin grafting. Sci Rep 2025; 15(1): 27814. DOI: 10.1038/s41598-025-95437-5.

[28] Mony MP, Harmon KA, Hess R, Dorafshar AH, Shafikhani SH. An updated review of hypertrophic scarring. Cells 2023; 12(5): 678. DOI: 10.3390/cells12050678.

[29] Yergoz F, Hastar N, Cimenci CE, Ozkan AD, Tekinay T, Guler MO, *et al.* Heparin mimetic peptide nanofiber gel promotes regeneration of full thickness burn injury. Biomaterials 2017; 134: 117-27. DOI: 10.1016/j.biomaterials.2017.04.040. Epub 2017 Apr 22. PMID: 28458029.

[30] Mohammadi Sardo H, Mirzaee F, Abbasnia SM, Seyedi M, Pourfridoni M. Heparin effect on wound healing and scar formation; recommendation of heparinized surgical suture threads to reduce scar: A practical hypothesis. Canon J Med 2024; 4(4): 97-9.

[31] Ayengin K, Kılıç N. Use of Contractubex® (Allantoin, Heparin, Extractum Cepae) to prevent scar formation in the rabbits to which primary closure has been applied after urethrotomy. East J Med 2020; 23(1): 161-9. DOI: 10.5505/ejm.2020.80948

Received: October 31, 2025 Revised: November 18, 2025 Accepted: November 24, 2025

© 2025. The Authors, National Journal of Health Sciences.
This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY- NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non- commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.